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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/566,911	02/03/2006	Bum Tae Kim	DE1672	1133

79681 7590 04/27/2009

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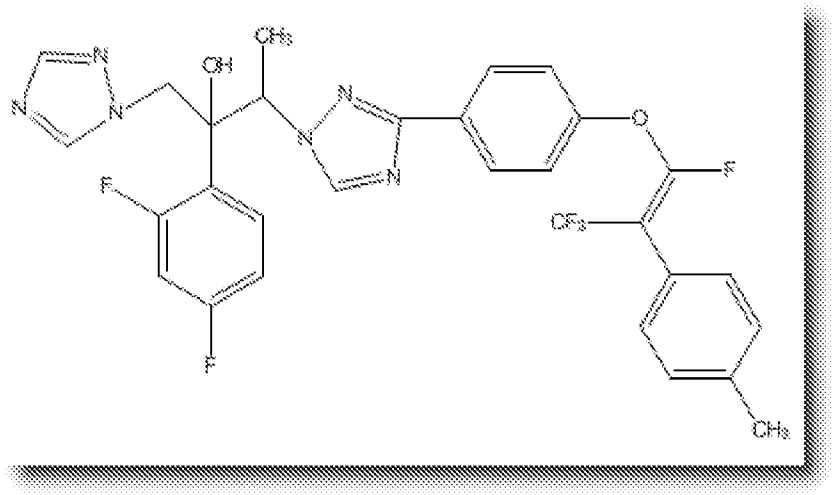
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
04/27/2009	PAPER

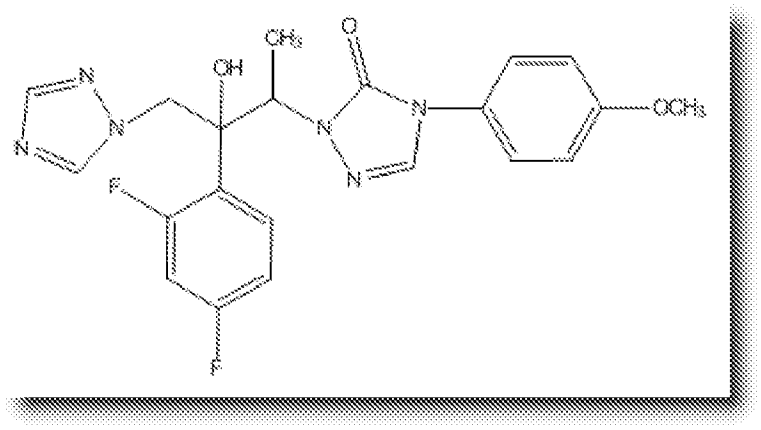
Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

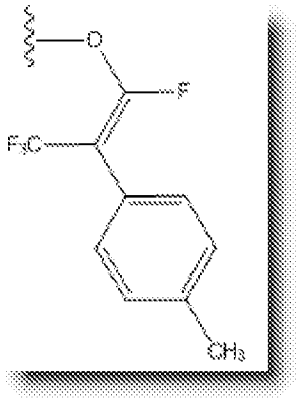
1. **The request for reconsideration has been considered but does NOT place the application in condition for allowance because**: The instant claims are drawn to compounds of formula (I) which encompass the following compound species:

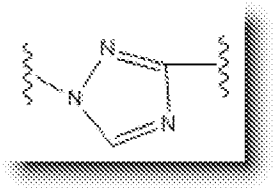


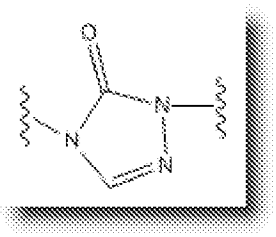
As discussed in a previous Action, *Itoh et al* teach the following structurally and functionally related antifungal compound



(Column 59, Table 9, No. 8). Although *Itoh et al* do not teach the compound recited by instant claim 1, it is noted that the compound of instant claim 1 differs from *Itoh et al* only in **(1)** the substitution of phenol with



(in the instant compound) as opposed to, for example, O-CH_3 (in *Itoh et al*) and **(2)** the replacement of 

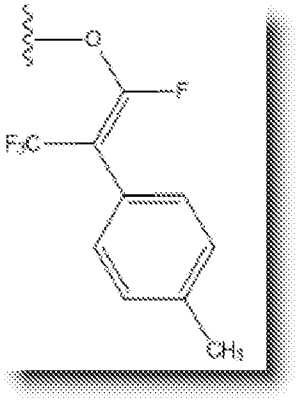
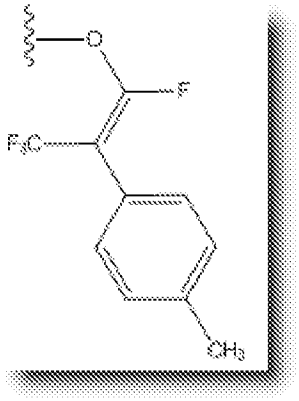
(in the instant compound) in place of 

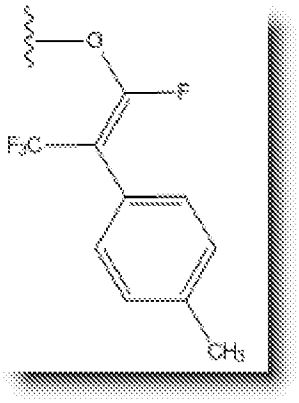
(in *Itoh et al*). However, as previously discussed, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to make the above modifications.

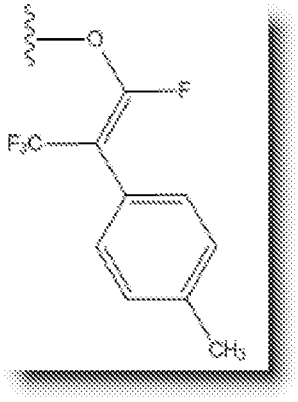
2. As to **(1)**, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the moiety in the compound taught by *Itoh et al* for the following reasons:

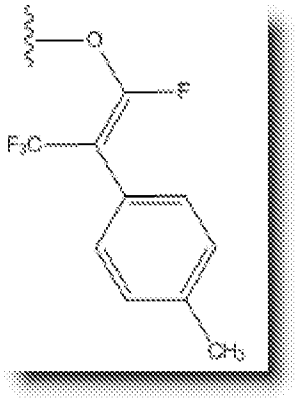
3. **FIRST**, *Itoh et al* teach that the compounds can be modified at phenol. For example, *Itoh et al* teaches modifications at phenol such as $–OCH_3$, $-OCF_3$, and $–O(CH)(CH_3)_2$ etc. Accordingly, it would have been obvious to a person of ordinary skill in the art to envisage modification of the compound taught by *Itoh et al* and, furthermore, it would have been obvious

to a person of ordinary skill in the art to envisage modifying the compound taught by *Itoh et al* at that specific position; namely, phenol.

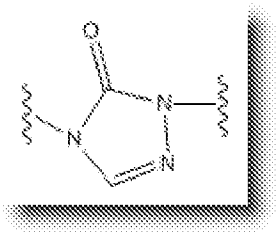
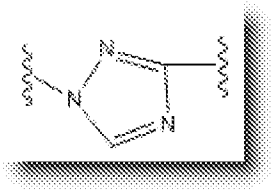
4. **SECOND**, *Kim et al* teach the group represented by  in fungicidal compounds (For example, Column 41, Example No. 105). More specifically, *Kim et al* teach "a fungicidal compound… having a fluorovinyl… moiety… useful for protecting crops from fungal diseases" (abstract). Accordingly, one of ordinary skill in the art at the time the invention was made would have recognized that compounds containing the group represented by  have fungicidal activity.

5. **THIRD**, *Kim et al* specifically provide the motivation to include the group represented by  in fungicidal compounds. Specifically, *Kim et al* teach that "the compounds of the present invention have a broad fungicidal activity spectrum against the target fungi when compared with the control compounds such as ORIBRIGHT and FENARIMOL" (Column 57, Lines 53-57). Notably, although ORIBRIGHT™ and FENARIMOL™ share some structural similarities with the compound disclosed by *Kim et all*, neither ORIBRIGHT™ nor FENARIMOL™ contain a fluorovinyl moiety. Accordingly, one of ordinary skill in the art at the time the invention was made would have recognized a motivation to include the moiety in compounds having antifungal activity.

6. **And FOURTH**, *Kim et al* teach that it is routine to react phenol with the group represented by  to generate compounds. Specifically, *Kim et al* teach the

reaction of the group represented by  with phenol in Reaction Scheme G (Column 12, Lines 50-65). As disclosed by *Kim et al*, the reaction as shown in Reaction Scheme G is carried out "according to a conventional method" (Column 12, Lines 45-49). Accordingly, one of ordinary skill in the art at the time the invention was made would have known to react the moiety at phenol.

7. Thus, based on *Kim et al* - which teach that compounds containing a fluorovinyl moiety exhibit enhanced fungicidal activity compared with compounds that lack the moiety - it would have been obvious to one of ordinary skill in the art at the time the invention was made to include a fluorovinyl moiety into the invention taught by *Itoh et al*, a known fungicidal, in an effort to enhance the fungicidal activity. Furthermore, it would have been obvious to a person of ordinary skill in the art to include the moiety at the phenol position in *Itoh et al* since *Itoh et al* teach that the phenol position is capable of being modified and additionally because *Kim et al* specifically teach the addition of the moiety at phenol.

8. As to **(2)**, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to replace  (in *Itoh et al*) with  (in the instant compound) for the following reasons:

9. *Boyle et al* teach antifungal compounds containing a non-oxygenated triazole attached to the identical core described by the instant application (entire document). More specifically, *Boyle et al* teach, for example, the following compounds with antifungal activity having a non-oxygenated triazole attached to the instant core:

Compound Number	R'	Activity: *C. albicans* in Vivo (μg/mL, IC_{80})	Activity: Antifungal Spectrum (μg/ml, MIC) Yeast	Myceliun	Dermatophyte	*C. albicans* in Vivo (mg/kg)	Half-life in Rat (days)
28	4-CN	0.12	100-1.6	0.01	100-1.6	1.0	1
36	4-$CONH_2$	0.53	>100	0.01	(100)	>25	
30	4-$CON(Me)CH_2C_6F_5$	0.006	25-6.2	<0.01	≤1.6	10	
29	4-OCF_3	0.05	6.2-1.6	<0.001	1.6	0.25	6.5
33	4-OCF_2CF_2H	0.004	100-1.6	<0.01	6.2-1.6	0.25	9
32	4-OCH_2CF_3	0.03	1.6	<0.01	1.6	0.5	1.5
34	4-$OCH_2CF_2CF_2H$	0.003	6.2-1.6	<0.01	≤1.6	0.25	1
31	4-OCH_2CH_2F	0.003	25-1.6	<0.001	1.6	25	
35	4-OCH_3	0.001	100-1.6	<0.01	25-1.6	>25	

(Page 97, Table 5). Accordingly, it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use compounds having either an oxygenated triazole (as

taught by *Itoh et al*) or a non-oxygenated triazole (as taught by *Boyle et al*). In doing so, the skilled artisan would have arrived at the instant compound.

10. Instant claim 3 is drawn to "a fungicidal composition comprising the compound according to claim 1 as an active ingredient and an inert carrier" (claim 3). *Itoh et al* specifically teach the compound "when it is used as an antifungal agent... is dissolved or dispersed in a suitable liquid carrier or mixed or absorbed with a suitable solid carried" (Column 14, Lines 47-52) and that "examples of the liquid carried used are water…" (Column 14, Line 63). Thus, *Itoh et al* specifically teach the compound which, as discussed above, is obvious in view of *Kim et al*, as an active ingredient with an inert carried in a fungicidal composition. Accordingly, claim 3 is obvious.

11. Applicant, however, argues that the antifungal compounds taught by *Itoh et al* are oxygenated. Yet, as discussed above, in view of *Boyle et al*, which teach structurally and functionally related compounds having a non-oxygenated triazole, the skilled artisan would have recognized that the oxygenation of the triazole is not critical to the compound's function, and that compounds having either an oxygenated triazole (as taught by *Itoh et al*) or a non-oxygenated triazole (as taught by *Boyle et al*) are alternatively usable.

12. Applicant further argues that *Boyle et al* do not disclose compounds having a phenol moiety attached directly to the triazole. This argument is not found persuasive because *Itoh et al* teach compounds wherein the (oxygenated) triazole is directly attached to a phenol moiety and the skilled artisan would have found it obvious to replace the oxygenated trizaole taught by *Itoh et al* with a non-oxygenated triazole in view of *Boyle et al*. The fact that the triazole is not directly connected to the phenol moiety in *Boyle et al* would <u>not</u> lead the skilled artisan to the

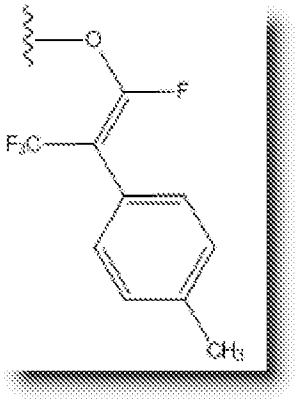
conclusion that the non-oxygenated triazole-containing compounds taught by *Boyle et al* are only functional when they are linked to the phenol moiety by a CH=CH linker. Indeed, as stated by MPEP 2144.09:

> A *prima facie* case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." *In re Payne*, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979).
>
> Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by $-CH_2-$ groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re Wilder*, 563 F.2d 457, 195 USPQ 426 (CCPA 1977).

Accordingly, the skilled artisan would have reasoned that compounds differing by the successive addition or subtraction of the same chemical group (i.e., a CH=CH linker) would be of sufficiently close structural similarity to have a presumed expectation that such compounds would possess similar properties. Thus, the fact that the triazole is not directly connected to the phenol moiety in *Boyle et al* would not lead the skilled artisan to the conclusion that the non-oxygenated triazole-containing compounds taught by *Boyle et al* are only functional when they are linked to the phenol moiety by a CH=CH linker, but rather, in view of *In re Payne* and *In re*

Wilder, the skilled artisan would have predicted that oxygenated triazole-containing compounds wherein the oxygenated triazole is attached directed to the phenol moiety would possess similar properties to the compounds taught by *Boyle et al*.

13. Applicant further argues that *Boyle et al* do not disclose compounds having flurovinyl moiety. This argument is not found persuasive because, as discussed previously and reiterated above, it would have been *prima facie* substitute the compounds taught by *Itoh et al* with a flurovinyl moiety (taught by *Kim et al*) and then to exchange the non-oxygenated triazole (taught by *Boyle et al*) in place of the oxygenated triazole taught by *Itoh et al*.

14. Applicant also argues that - although *Kim et al* teaches the flurovinyl moiety - they do not teach the core structure of the instant compound. Although it is true that Kim et al do not teach the core structure of the instant compound, they do pecifically provide the motivation to include the group represented by  in fungicidal compounds, such as those taught by *Itoh et al* in view of *Boyle et al* (and thus having the core structure of the instant compound) for the reasons previously dicussed. Specifically, *Kim et al* teach that "the compounds of the present invention have a broad fungicidal activity spectrum against the target fungi when compared with the control compounds such as ORIBRIGHT and FENARIMOL" (Column 57, Lines 53-57). Notably, although ORIBRIGHT™ and FENARIMOL™ share some structural

similarities with the compound disclosed by *Kim et all*, neither ORIBRIGHT™ nor FENARIMOL™ contain a fluorovinyl moiety. Accordingly, one of ordinary skill in the art at the time the invention was made would have recognized a motivation to include the moiety in compounds having antifungal activity, such as those taught by *Itoh et al* in view of *Boyle et al.*

15. Finally, Applicant's argument that the instant compounds have high antifungal activity and low toxicity to minimize hepatic toxicity and toxicity of oral administration appears to be based on limitations which are not present in the claims. No where in the claims does Applicant recite that the azole derivatives of formula (I) are of low toxicity or useful for humans for oral administration. Accordingly, these limitations are not accorded patentable weight. The skilled artisan would have been motivated to combine the teachings of *Itoh et al* with *Kim et al* and *Boyle et al* to enhance the fungicidal activity of the compounds taught by *Itoh et al* with a reasonable expectation of success. Since *Itoh et al* clearly teach that the compounds disclosed can be "used as an antifungal agent for agricultural purposes" (Column 14, Lines 48-49) the skilled artisan would have readily looked to *Kim et al* for guidance.

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614